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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/850,199 | 05/08/2001 | Helen Fillmore | 18377-0034 | 9734 |

29052 7590 10/15/2004

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| EXAMINER | |
|---|---|
| FREDMAN, JEFFREY NORMAN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1637 | |

DATE MAILED: 10/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/850,199 | FILLMORE ET AL. | |
| | Examiner | Art Unit | |
| | Jeffrey Fredman | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 August 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 19, 2004 has been entered.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

Here, claims 1-4 contain prohibited new matter. Specifically, the new phrase "non-viral" lacks any basis in the specification. A careful review by the examiner of the

cited pages of the specification by the applicant failed to identify any support for this new negative limitation. The particular cited sections never use the phrase "non-viral", or specifically state that the vector is not a viral vector. As noted by MPEP 2173.05(I),

> " Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

There is no basis for the exclusionary proviso. At best, and not persuasively, Applicant's arguments would indicate that there is an absence of a positive recitation. Since no basis has been found to support the new claim limitation in the specification, the claim is rejected as incorporating new matter.

***Claim Rejections - 35 USC § 102***

4. The rejections of claims 1, 2 and 4 under 35 U.S.C. 102(b) are withdrawn in view of the amendment requiring the vector to be bicistronic.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rees et al (Biotechniques (1996) 20:102-110) in view of in view of Cheng et al (Gene Therapy (1997) 4:1013-1022).

8. Rees teaches a non-viral bicistronic DNA vector construct (see page 104, figure 1) comprising:

a) an internal ribosomal entry site (IRES) (see page 104, figure 1),

b) a selection marker (see page 104, figure 1,where there is an NEO selectable marker under the control of the IRES element),

With regard to claims 2 and 4, Reese teaches "To facilitate the creation of stable cell lines, we have developed a bicistronic expression vector the predisposes every transfected cell to express recombinant protein and at apparently high levels (see page 102, column 3)."

Rees does not teach placement of the GFP into the vector nor placement into stem cells.

Cheng teaches a DNA vector construct (see page 1014, figure 1) comprising:

a) an internal ribosomal entry site (IRES) (see page 1014, figure 1, MGIN vector with IRES element and column 2),

b) a selection marker (see page 1014, figure 1, where NEO is a selection marker in the MGIN vector),

c) a green fluorescent protein marker (see page 1014, figure 1, where EGFP is a green fluorescent protein marker).

With regard to claim 2, Cheng teaches "GFP expression in MGIN transduced TF1 cells was stable since GFP-expressing TF1 cells (which were selected either by resistance to G418 or by FACS for GFP fluorescence) continued expressing EGFP at a high level for more than 2 months in the absence of G418 selection (see page 1014, column 2)." Thus, Cheng teaches stably transfected cells with the vector of claim 1.

With regard to claim 3, Cheng teaches "We report the development of a reporter system using EGFP for the analysis of conditions leading to optimal retrovirus mediated gene transfer into human primitive hematopoietic progenitors (see page 1014, column 1)". Thus, Cheng teaches stably transfection of stem cells (see page 1015, column 2).

With regard to claim 4, Cheng teaches the reagent which is the cells as discussed in claim 2. Cheng expressly uses the reagent to study biological processes (see page 1016, column 2, subheading "Effect of GFP expression on biological properties of transduced HSPC").

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the Rees vector with GFP in the place of the Cheng vector for formation of stably transfected cells since Rees notes that the vector is superior to viral vectors, commenting "In contrast" (to viral vectors) "we have shown that following transfection with pCIN, every cell line characterized expresses recombinant

protein and at apparently high levels. Furthermore, the use of neomycin rather than DHFR within a bicistronic mammalian expression vector should greatly increase the versatility of such vectors (see page 109, column 3)." So an ordinary practitioner, interested in a convenient method of expressing their protein of interest in a stable way in mammalian cells would have modified the vector of Cheng, which contained both Neo and EGFP to form a bicistronic vector as taught by Rees. Further motivation to place the EGFP into expression vectors is provided by Cheng, who extols the GFP as "readily detectable in many transiently transfected cells (see page 1014, column 1)." Cheng further notes that the EGFP is hundreds fold more sensitive than GFP (Cheng notes that a previous EGFP mutant is 35 fold more sensitive and his mutant is 17 fold more sensitive than the previous mutant, so it must be 595 fold more sensitive than GFP). Motivations to modify the use of the vector of Rees, with GFP and Neo as taught by Cheng, include the teaching by Rees that such a vector will "permit the rapid and efficient production of stable mammalian cell lines for the characterization of recombinant protein, as this vector appears to predispose all transfected cells to express such protein (see abstract)." Thus, for all of these reasons, an ordinary practitioner would have been motivated to for bicistronic vectors with Neo and GFP as taught by Cheng in the IRES vector of Rees in order to permit the rapid and efficient production of stable mammalian cell lines, a goal of both Rees and Cheng.

***Response to Arguments***

9. Applicant's arguments filed August 19, 2004, have been fully considered but are not considered persuasive.

Applicant first argues the new matter rejection regarding the language "non-viral". Applicant argues that the language describes a "non-viral DNA vector". The argument is not persuasive for several reasons. First the vector shown in the example could be termed a "bacterial" vector because it has the origin of replication necessary to replicate in bacterial cells. However, to say that a description of a plasmid vector supports the significantly more generic term "non-viral vector" is not persuasive. There are non-viral vectors other than bacterial vectors such as vectors for insect cells and chromosomal vectors for yeast. Alternatively, there are vectors that may be termed "viral", but which lack any significant viral character since they are stripped of any proteins which permit viral replication. So when a specification nevers uses the term "non-viral" and has no positive recitation of the limitation, the argument that a narrower subgeneric element is shown does not provide descriptive support for the broader negative recitation of "non-viral".

Applicant then argues the prior art rejections. Because a new prior art rejection was necessitated by Applicant's amendment, the arguments are moot with regard to the new rejection.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
9/28/07